Annals of Clinical and Analytical Medicine
Original Research

Sepsis-Related Mortality with SOFA and qSOFA in Emergency Department Patients

Sepsis-related mortality in emergency department

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Abstract
Aim: Prediction of sepsis-related mortality in the emergency department (ED) is important. In this study, we aimed to assess the predictive power of the newly defined scoring systems in sepsis-related mortality and reduce it in the ED.
Materials and Methods: A prospective cohort study was conducted on a sample of patients who presented to the ED with sepsis. Patients aged <18 years and those with shock from non-septic causes were excluded. Age, vital signs, laboratory findings on admission, culture time, time of empiric antibiotic therapy, results of scoring systems, duration of ED stay and hospitalization, focus of infection and clinical outcome were recorded.
Results: A total of 48 patients were enrolled in the study. SOFA scores were higher in patients who died (p = 0.001, 95% CI, 0.639–0.902). The best cut-off point for diagnostic performance was a SOFA score of 4.5. At this point, sensitivity was 82.61%, specificity was 56.0%, positive predictive value was 63.3% and negative predictive value was 77.8%.
Discussion: qSOFA and SIRS cannot provide adequate prognostic information in the ED, whereas, SOFA reliably predicted mortality. Our results indicate that vital signs are more flexible and efficient data sources. Although it is presently not precisely understood how RDW is associated with clinical outcomes but patients with increased RDW levels should be more aggressively treated and admission RDW could also be used for prognostic purposes, particularly in busy EDs. Also, lactate levels were correlated with SOFA and qSOFA scores and that the former could predict mortality (p= 0.012) is consistent with previous studies of infection
Conclusion: In conclusion, qSOFA had poor performance for the prediction of sepsis-related mortality in the ED. SOFA had the best performance.

Keywords
Sepsis; SOFA; qSOFA; Emergency Department; Mortality

DOI: 10.4328/ACAM.20079 Received: 2019-11-23 Accepted: 2019-12-23 Published Online: 2019-12-28 Printed: 2020-09-01 Ann Clin Anal Med 2020;11(5):359-364
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Introduction

Sepsis refers to organ dysfunction threatening the host's life that results from an impaired host response elicited by the culprit infection and remains a major concern in ED as a result of determining the mortality in one-hour-therapeutic management, so the emergency physicians play a major role [1, 2]. Delay in adequate treatment, subsequently impacts mortality and cost in sepsis [3].

According to Sepsis 3, SOFA is mainly a clinical diagnostic criterion; qSOFA is a screening tool to predict sepsis-related outcomes [3-5]. Recently many studies have tried to figure out the diagnostic and prognostic value of these newly defined scoring tools [6–10]. No consensus has been reached, because some studies are based on the ED septic patients and others on patients seen outside. Because emergency physicians are the first to encounter patients with sepsis, tests and tools that can be used for bedside diagnostic and prognostic purposes are desirable.

We conducted a study to assess the predictive power of the newly defined scoring systems SOFA and qSOFA compared with traditional SIRS criteria for sepsis-related mortality in the ED patients.

Material and Methods

This single-center, prospective cohort study was assessed between November 1, 2017 and March 31, 2018 in the ED of an academic tertiary care hospital. The study was approved by the local ethics committee. Consent for participation in the study was obtained from the patients or from the relatives of patients who could not give consent because of unconsciousness, mental retardation, psychiatric illness, or Alzheimer's or other dementia.

Data were obtained from hospital electronic records and patient follow-up forms. The subjects were examined by ED physicians for assessment and fulfillment of the clinical criteria for severe sepsis or septic shock according to the guidelines of the Surviving Sepsis Campaign and were subsequently admitted to the hospital between the dates indicated (n = 187). Patients who were diagnosed with sepsis and hospitalized or discharged from the ED were included in the study. The extracted data included the presence of SIRS criteria, the qSOFA and SOFA scores and the time required to meet the criteria. We excluded patients younger than 18 years, patients referred from outside facilities and patients with shock from non-septic causes, such as cardiogenic shock, left heart failure, right heart failure, arrhythmia, acute coronary syndrome, pulmonary embolism, tension pneumothorax, cardiac tamponade, hypovolemic shock, vasodilatory (distributive) shock, neurogenic (spinal) shock, adrenal shock and anaphylaxis.

A study form was used that included age, vital signs (blood pressure, heart rate, body temperature, oxygen saturation and shock index) and laboratory findings (complete blood count, biochemistry and blood gas measurements) on admission and culture time, time of empiric antibiotic therapy, results of scoring systems (SOFA, qSOFA, and SIRS), duration of ED stay and hospitalization, focus of infection and in-hospital mortality. Chart reviews were completed by trained emergency physician researchers (following predetermined guidelines defining abstraction criteria) to determine the presence and timing of the various components of the SIRS, qSOFA, and SOFA criteria. The qSOFA criteria were altered mental status, respiratory rate (RR)>22/min and systolic blood pressure (SBP)>100 mmHg. The SIRS criteria were heart rate (HR)>90 bpm, white blood cell (WBC) count >12,000/dL or<4000/dL, RR>20/min, temperature >38.5°C or <36°C, and a five-degree SOFA score consisting of respiratory (PaO2/FiO2[mmHg]), coagulation (platelets [*103mm3]), hepatic (bilirubin [mg/dL]), cardiovascular (hypotension, defined as mean arterial pressure ≤65 mmHg and need for vasopressor support), central nervous system (Glasgow Coma Scale) and renal (creatinine [mg/dL]) functions.

The sample size required to achieve our objectives was primarily determined by the accuracy (width of the confidence interval around the point estimate of sensitivity) of SOFA for the primary outcome. Before the study, we estimated that the mean SOFA score would be approximately 4±2 in the surviving group and 6 in the deceased group. Based on these values, the required sample size was 16 for each group, with a type1 error of 0.05 and a power of 80%. The mean SOFA score was 4.56±2.66 in the surviving group and 8.61±4.43 in the deceased group. According to these scores, the minimum sample size was 7 for each group, with a type1 error of 0.05 and a power of 80%.The patient flow is shown in Figure 1.

Statistical analysis was performed with SPSS version 23.0 software (SPSS Inc., Chicago,IL, USA). For the variables, a normal distribution was determined using the one-sample Kolmogorov-Smirnov test; continuous variables that were not normally distributed were expressed as medians (min–max), and categorical variables were expressed as numbers and percentages. The Mann-Whitney U test was used to compare continuous variables between two groups. The significance of differences between categorical variables was calculated using the Chi-Square test. Correlations between two continuous variables were calculated by the Spearman's rank correlation coefficient (rho). Coefficients between 0 and 0.3 indicated weak correlation, coefficients between 0.3 and 0.7 indicated moderate correlation and coefficients between 0.7 and 1 indicated strong correlation. Comparison of prognostic performances of SOFA and qSOFA with SIRS and the influence of the continuous SOFA score on mortality was performed by receiver operating characteristic (ROC) analyses; the best cut-off point was determined as the point at which the sum of sensitivity and specificity was the greatest. P-values <0.05 were considered to indicate statistical significance.

Results

A total of 48 patients presenting to our ED with sepsis were eligible for this study. The mean age was 69.25±15.38 years (minimum, 22; maximum, 94). The most common site of infection was the pulmonary system (n=20, 41.7%), and the least common site was the central nervous system (n=1, 2.1%). qSOFA was ≥2 in 25 patients (52.1%), SOFA was ≥2 in 45 patients (93.7%) and SIRS was ≥ in 38 patients (79.1%).

Tables 1 and 2 show the predictive values of variables affecting mortality. Initial red cell distribution width (RDW), aspartate aminotransferase (AST), lactate and base deficit (BD) were greater in patients who died (p = 0.001, 0.014, 0.012 and 0.003,

respectively), whereas bicarbonate (HCO3) and fever were lower (p=0.003 and 0.002, respectively) (Table 1). Among patients who died, SOFA scores were greater (p=0.001) and hospital stay was shorter (0.016) (Table 2).

Correlations of variables with the scoring systems are shown in Table 3. SBP, fever, glomerular filtration rate (GFR) and BD had moderate negative correlations with SOFA score, while the Glasgow Coma Scale (GCS), mean platelet volume (MPV), blood urea nitrogen (BUN), creatinine and lactate had moderate positive correlations with SOFA score. Age and GCS had moderate positive correlations and MPV and lactate had weak positive correlations with qSOFA. HR, RR, fever and platelet count had moderate positive correlations and SO2 had a moderate negative correlation with SIRS.

Overall, in-hospital mortality was 47.9% (n= 23). The ROC curve of the SOFA score for predicting mortality is shown in Figure 2 (AUC=0.770; p=0.001; 95% CI, 0.639–0.902). Based on diagnostic performance, the best cut-off point was a SOFA score of 4.5. However, we cannot use a SOFA score of 4.5 as a cut-off because it is not an integer. We calculated the mortality rates above and below a SOFA score of 4. At this point, the mortality rate was 62.5%, the sensitivity was 82.61%, the specificity was 56.0%, the positive predictive value was 63.3% and the negative predictive value was77.8% (Figure 2).

According to our results, qSOFA and SIRS cannot provide adequate diagnostic and prognostic information in the ED (Table 2). In contrast, SOFA reliably predicted mortality (Figure 2).

Discussion

Recent studies comparing sepsis scores have produced different results [11–14]. According to our results, while maintaining the value of SOFA in predicting mortality, qSOFA scores could not identify patients with the most severe forms of infection early in the course in the ED. The latter result is inconsistent with previous studies on the use of qSOFA to predict patients with increased risk of prolonged stay in the intensive care unit or death [11, 15].

Although several scoring systems exist to assess the prognosis in critically ill patients, they are difficult to apply in patients presenting to acute care because of time constraints. Vital signs can provide important prognostic information in patients with acute illness [16]. We found that haemoglobin, fever, and GCS correlated well with SOFA and qSOFA (r = 0.349, 0.412, and 0.692 respectively), indicating that vital signs are more flexible and efficient data sources.

The sepsis-induced inflammatory milieu and organ damage ultimately resulting in death have been poorly described. The liver is the laboratory of the human body, which is capable of performing more than 200 functions, including detoxification, storage, energy production, nutrient conversion, hormonal balance and coagulation, all of which render the liver a critical organ in sepsis [17]. The liver plays prominent roles in the septic process, such as removing bacteria, mediating the inflammatory response and regulating coagulation, which may play a role in the pathogenesis of renal failure, acute lung injury, acute respiratory distress syndrome, coagulopathy and hepatic encephalopathy. The liver is vulnerable to injury from pathogens, toxins, and inflammatory compounds, which may lead to hepatocellular dysfunction, hepatic injury, and ultimately hepatic failure [18]. Septic injuries to the liver can be broadly classified as hypoxic hepatitis or the jaundice type. The latter is the more common type and is the main component of SOFA, which should be assessed as a part of the overall clinical presentation [19]. Rise in hepatic transferase is not sufficient when the use of SOFA is contemplated in the ED, as shown in our study.

It is presently not precisely understood how RDW is pathophysiologically formed and associated with clinical outcomes. However, it is known that RDW is elevated by inflammatory processes that interfere with iron metabolism, augment erythrocyte apoptosis, decrease erythropoietin production and suppress bone marrow [20, 21]. We found a significantly higher RDW level in patients who died (p=0.001), suggesting that patients with increased RDW levels should be more aggressively treated and admission RDW could also be used for prognostic purposes, particularly in busy EDs.

Although the role of MPV in sepsis is not fully understood, it has been reported to remain at normal levels in localized bacterial infections, but to be significantly elevated in half of patients with sepsis [22]. We found that MPV was positively correlated with SOFA and qSOFA scores (r = 0.313 and 0.93, respectively) and according to previous reports [23] impaired thrombocyte production and function caused by the impact of sepsis on bone marrow may be reflected in MPV as an indirect sign of dysfunction; this parameter can be used in the ED as a quick and reliable sign of sepsis.

We found that lactate levels were correlated with SOFA and qSOFA scores and that the former could predict mortality (p= 0.012), this result is consistent with previous studies of infection [24]. At present, although the use of three scoring systems cannot be universally recommended, lactate measurements should be combined with them when an infection is suspected.

Limitations

The most obvious limitation of this research was that of a small sample size. Although the sample size was small, we adequately addressed the research questions or generalized beyond the context of the study and still, the small population did not negate recognition of importance of SOFA in predicting sepsis-related mortality in ED, but with a larger sample, including a greater number of culturally different participants any real differences would almost certainly have emerged. Our study produced statistically significant results concerning sepsis scoring systems and encouraged to find results similar to larger and more inclusive studies. Secondly, baseline information on cardiovascular risk factors, comorbidities and concurrent medication, which were important potential confounders in this context, was not collected or available to the data extractors, and any potential influence on vital signs was not controlled. Larger, multisite, prospective studies are needed to control for multiple confounders and find clinically important associations.

Conclusion

In conclusion, this study highlighted the poor performance of qSOFA and the reliable performance of SOFA for the prediction of sepsis-related mortality in the ED. We hope this small study will provoke more investigation into the appropriateness of fully adopting mortality predicting sepsis scores as a screening tool by emergency medicine physicians.

Table 1. Prognostic value of vital signs and laboratory variables on admission

Variable	Total (n = 48)	Survivors (n = 25)	Deceased (n = 23)	p
	n (%) or median (minimum–maximum)			
Age (yr)	68 (22–94)	68 (22–89)	70 (49–94)	0.967
SBP (mmHg)	98.5 (60–190)	102 (60–183)	90 (72–190)	0.129
HR(beats/min)	100 (56–170)	105 (59–145)	99 (56–170)	0.932
RR(breaths/min)	22 (12–40)	23.5 (15–40)	21.5 (12–40)	0.303
Fever (°C)	36.9 (36–39.8)	37.4 (36–39.8)	36.3 (36–38.1)	0.002
sO2 (%)	88 (56–98)	90 (56–98)	87.5 (60–97)	0.741
Shock index	1 (0.3–2.8)	1 (0.3–2)	1.1 (0.3–2.8)	0.304
GCS				
14–15	19 (39.6%)	13 (52%)	6 (26.1%)	0.166
11–13	15 (31.3%)	8 (32%)	7 (30.4%)	
10	3 (6.3%)	1 (4%)	2 (8.7%)	
7–9	4 (8.3%)	2 (8%)	2 (8.7%)	
<6	7 (14.6%)	1 (4%)	6 (26.1%)	
WBCs	16.2 (1.1–39.3)	17.8 (1.1–39.3)	12.5 (2.9–31.3)	0.332
Neutrophils	86.1 (11.4–96.6)	86.8 (36.1–96)	84.7 (11.4–96.6)	0.450
Haemoglobin	11.8 (6–18.4)	11.1 (7.4–18.4)	12.5 (6–16.3)	0.403
Haematocrit	36.8 (19.6–54.8)	34.7 (22.4–54.8)	41.7 (19.6–53.3)	0.288
Platelets	229.5 (67–928)	277 (73–928)	199 (67–646)	0.212
MPV	10 (8–13)	10 (9–13)	11 (8–13)	0.529
RDW	48.5 (16.1–69.8)	46.9 (16.1–69.8)	53.3 (39.2–68.1)	0.001
ALT	19 (5–405)	18 (5–249)	20 (5–405)	0.173
AST	24 (6–954)	19 (6–210)	32.5 (12–954)	0.014
Total bilirubin	0.29 (0.09–4.26)	0.23 (0.11–4.15)	0.37 (0.09–4.26)	0.140
Creatinine	1.52 (0.26–10.23)	1.07 (0.26–9.48)	1.83 (0.43-10.23)	0.054
BUN	79.5 (17–494)	58 (17–282)	92 (17–494)	0.148
GFR	42 (3–201)	58 (3–201)	31 (5–134)	0.151
PaO2	47 (30.9–78)	49 (31.1–77.3)	44.6 (30.9–78)	0.757
HCO3	20 (7.4–32.6)	23.5 (7.4–32.6)	17.1 (8.2–29.3)	0.003
Lactate	2.65 (0.7–13.2)	2.1 (0.7–7.3)	3.7 (1.7–13.2)	0.012
BD	−4.2 (−20.2 to 5.8)	−0.75 (−17.9 to 4.3)	−7.2 (−20.2 to 5.8)	0.003

SBP: systolic blood pressure; HR: heart rate; RR: respiratory rate; sO2: oxygen saturation; GCS: Glasgow Coma Scale; WBCs: white blood cells; MPV: mean platelet volume; RDW: red cell distribution width; ALT: alanine aminotransferase; AST: aspartate aminotransferase; BUN: blood urea nitrogen; GFR: glomerular filtration rate; PaO2: arterial oxygen pressure; HCO3: bicarbonate; BD: base deficit.

Table 2. Prognostic value of clinical variables and scoring systems

Variable	Total (n = 48)	Survivors (n = 25)	Deceased (n = 23)	p
	n (%) or median (minimum–maximum)			
Culture time				
1st 1 h	16 (34.8%)	12 (48%)	4 (19%)	0.101
3 h	12 (26.1%)	6 (24%)	6 (28.6%)	
>3 h	18 (39.1%)	7 (28%)	11 (52.4%)	
Start of antibiotics				
<1 h	11 (23.9%)	8 (32%)	3 (14.3%)	0.411
<3 h	8 (17.4%)	4 (16%)	4 (19%)	
<6 h	10 (21.7%)	6 (24%)	4 (19%)	
>6 h	17 (37%)	7 (28%)	10 (47.6%)	
SOFA	6 (0–17)	4 (0–9)	7 (2–17)	0.001
qSOFA	2 (0–3)	1 (0–3)	2 (0–3)	0.191
SIRS	2 (0–4)	3 (0–4)	2 (1–4)	0.155
Emergency department stay time				0.332
<24 h	18 (37.5%)	11 (44%)	7 (30.4%)	
>24 h	30 (62.5%)	14 (56%)	16 (69.6%)	
Hospital stay time (days)	4 (1–26)	9 (1–26)	1 (1–15)	0.016
Source of infection				
CNS	1 (2.1%)	0 (0%)	1 (4.3%)	0.724
Pulmonary	20 (41.7%)	9 (36%)	11 (47.8%)	
Abdominal	4 (8.3%)	2 (8%)	2 (8.7%)	
Urinary	17 (35.4%)	10 (40%)	7 (30.4%)	
Soft tissue	2 (4.2%)	2 (8%)	0 (0%)	
Multiple	2 (4.2%)	1 (4%)	1 (4.3%)	
Undefined	2 (4.2%)	1 (4%)	1 (4.3%)	
Vasopressin use	28 (58.3%)	12 (48%)	16 (69.6%)	0.130
PaO2/FiO2				
≥400	10 (20.8%)	7 (28%)	3 (13%)	0.071
<400	10 (20.8%)	7 (28%)	3 (13%)	
<300	8 (16.7%)	5 (20%)	3 (13%)	
<200	16 (33.3%)	6 (24%)	10 (43.5%)	
<100	4 (8.3%)	0 (0%)	4 (17.4%)	

SOFA: Sequential Organ Failure Assessment; qSOFA: quick SOFA; SIRS: Systemic Inflammatory Response Syndrome; CNS: central nervous system; PaO2: arterial oxygen pressure; FiO2: fraction of inspired oxygen.

Table 3. Correlation of variables and scoring systems

	SOFA		qSOFA		SIRS	
	r	p	r	p	r	p
Hospital stay time	−0.098	0.563	0.004	0.983	0.226	0.179
Age	0.180	0.222	0.317	0.028	−0.076	0.609
SBP (mmHg)	−0.349	0.015	−0.257	0.078	0.226	0.123
HR (beats/min)	0.044	0.767	0.055	0.713	0.453	0.001
RR (breaths/min)	−0.215	0.183	0.139	0.392	0.331	0.037
Fever (°C)	−0.412	0.004	−0.069	0.645	0.410	0.004
sO2 (%)	−0.155	0.297	−0.173	0.245	−0.347	0.017
Shock index	0.239	0.101	0.199	0.175	−0.048	0.748
GCS	0.692	<0.001	0.600	<0.001	−0.075	0.613
WBCs	0.169	0.250	0.077	0.605	0.202	0.169
Neutrophils	0.022	0.884	−0.054	0.718	0.161	0.280
Haemoglobin	−0.017	0.911	0.125	0.396	−0.058	0.697
Haematocrit	−0.007	0.963	0.131	0.375	−0.051	0.732
Platelets	−0.189	0.199	−0.002	0.990	0.313	0.030
MPV	0.313	0.032	0.293	0.046	−0.206	0.164
RDW	0.277	0.056	0.128	0.385	0.002	0.992
ALT	−0.047	0.750	−0.059	0.692	0.125	0.399
AST	0.079	0.608	−0.014	0.927	−0.035	0.819
Total bilirubin	0.042	0.786	−0.148	0.331	−0.084	0.583
Creatinine	0.448	0.001	.405**	0.004	0.062	0.674
BUN	0.316	0.029	.300*	0.039	0.200	0.172
GFR	−0.401	0.005	−0.423	0.003	−0.188	0.202
PaO2	−0.264	0.069	−0.272	0.061	−0.106	0.475
HCO3	−0.257	0.081	−0.096	0.521	−0.034	0.819
Lactate	0.371	0.011	0.293	0.048	−0.011	0.941
BD	−0.305	0.037	−0.168	0.258	−0.061	0.684

SOFA: Sequential Organ Failure Assessment; qSOFA: quick SOFA; SIRS: Systemic Inflammatory Response Syndrome; r: Spearman rho coefficient; SBP: systolic blood pressure; HR: heart rate; RR: respiratory rate; sO2: oxygen saturation; GCS: Glasgow Coma Scale; WBCs: white blood cells; MPV: mean platelet volume; RDW: red cell distribution width; ALT: alanine aminotransferase; AST: aspartate aminotransferase; BUN, blood urea nitrogen; GFR: glomerular filtration rate; PaO2: arterial oxygen pressure; HCO3: bicarbonate; BD: base deficit.

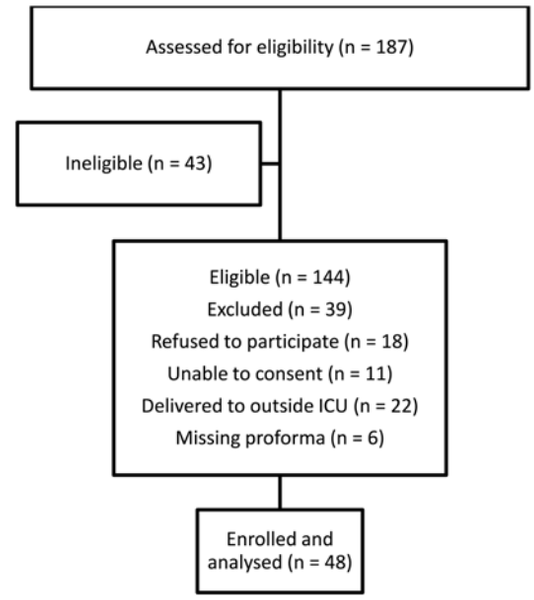

Figure 1. Flow chart of the patients.

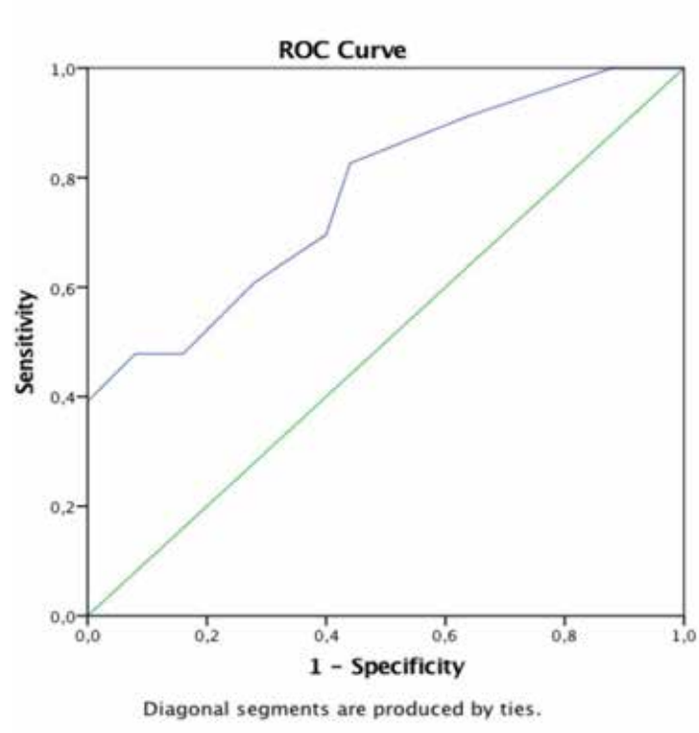

Figure 2. Receiver operating characteristic (ROC) curve of Sequential Organ Failure Assessment (SOFA) score for predicting mortality (AUC = 0.770; p=0.001; 95% CI, 0.639–0.902).

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

Funding: *None*

Conflict of interest
None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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How to cite this article:
Bedriye Müge Sönmez, Aysel Kocagül Çelikbaş. Sepsis-Related Mortality with SOFA and qSOFA in Emergency Department Patients. Ann Clin Anal Med 2020;11(5):359-364